REMARKS

Claims 34-65 are pending in the present application and independent claims 34, 52, 64 and 65 have been amended to particularly point out and distinctly claim certain embodiments encompassed by the invention and without prejudice to the prosecution of any subject matter removed by such amendments in any related continuation, continuation-in-part or divisional application. Dependent claim 49 and independent claim 64 have been amended solely to correct inadvertent typographical errors and in a manner that provides grammatical and logical consistency. Support for the present amendments may be found in the application (including the Drawings) as originally filed, for example, in the specification at page 7, line 6 through page 8, line 17; at page 9, line 23 through page 10, line 18; and elsewhere. No new matter is introduced by way of the present amendment.

REJECTIONS UNDER 35 U.S.C. §103

Claims 34-65 stand rejected under 35 U.S.C. §103 for alleged obviousness over Kreimer *et al.* (US 2001/0053521 A1, hereinafter "Kreimer") in view of Kreimer *et al.* (US 2003/007319, hereinafter "Kreimer02"). The PTO also asserts that claims 40, 41 and 58-60 are obvious over Kreimer in view of Chan *et al.* (US 2003/0231304 A1, hereinafter "Chan"), and that claims 40-42 and 58-60 are obvious over Kreimer in view of Kreimer02 and further in view of Chan *et al.* More specifically, the Examiner concedes with regard to independent claims 34, 52, 64, and 65 that Kreimer does not teach all the recited features, including the use of a second laser to enhance Raman scattering, but asserts that Kreimer02 teaches a system for measuring analytes by Raman scattering and surface plasmon resonance (SPR) using two independent light sources to perform independent surface enhanced Raman scattering (SERS) and SPR measurements. From this combination of teachings, the Examiner alleges that it would have been obvious to direct two light sources for SERS and SPR onto the same analyte to enhance the Raman signal emanating from the analyte.

Applicants respectfully traverse these grounds for rejection. The presently claimed embodiments are directed in pertinent part to a detector for detecting the presence of a molecule in an analyte on an analyte carrier having a conducting surface for receipt of an analyte

in an analysis region of the surface, comprising a first laser radiation source arranged to provide radiation directed, in use, to the analysis region to cause Raman scattering; a first sensor arranged to detect radiation from the first laser radiation source that has been scattered from the analysis region by Raman scattering to detect the presence of the molecule; a second laser radiation source arranged to provide radiation, in use, to the conducting surface at an angle to the conducting surface such that a field is generated in the analysis region; wherein the first and second laser radiation sources and the conducting surface and wavelength of the second radiation source are arranged such that the field generated by the second laser source matches a molecular vibrational energy state and thereby causes an enhanced Raman scattering effect of radiation of the first laser source; and to related embodiments.

The prior art fails to teach or suggest a second laser source that *matches* a molecular vibrational energy state and thereby causes an *enhanced* Raman scattering effect of radiation of the first laser source.

As disclosed throughout the present application and recited in the claims, the instant embodiments relate to the combination of (i) a first laser that causes Raman scattering that is detected by a first sensor which detects presence of an analyte molecule, and (ii) a second, field-generating laser that *enhances* the ability to detect the analyte molecule by the Raman scattering effect of (i), where such enhancement is obtained expressly by generating, with the second laser, a field that *matches* a molecular vibrational energy state of an analyte molecule that is in a higher energy state as a result of having absorbed laser radiation from the first laser (*e.g.*, by having absorbed a photon, such that Raman scattering occurs).

Such unprecedented enhancement of the Raman scattering effect results from the increased efficiency of energy transfer between the Raman-excited molecule of (i) and the *matched* field of (ii). See specification at, *e.g.,* page 7, line 29 through page 8, line 17. The presently recited combination thus overcomes the problem of poor signal-to-noise ratios in surface enhanced Raman scattering detection in a manner that is not even remotely suggested by Kreimer, Kreimer02 and/or Chan, whether taken alone or in any combination.

Applicants traverse in particular the Examiner's allegation of obviousness found in the Action at page 3, lines 13-16. It is submitted that the PTO fails to provide evidence or

reasoning as to why a person having ordinary skill in the art at the time of filing the present application would have had any reasonable expectation of successfully using a second laser that has been selected or tuned to generate a field to *match* a molecular vibrational energy state that had been caused in a Raman-excited analyte molecule by a first laser, thereby to *enhance* the Raman scattering effect caused by the first laser. On this point, the PTO impermissibly employs hindsight by reconstructing the prior art in view of the present application. Contrary to the assertion found in the Action, applicants submit that prior to the instant application the art failed to consider the possibility of SPR-assisted enhancement of Raman scattering.

Briefly, and to clarify the principles underlying the claimed invention embodiments, Raman scattering occurs when a photon is absorbed by a molecule and the molecule is excited to a higher energy state (or virtual state), and then decays to a state other than the ground state. The scattered photon emitted as a result of the decay has an energy value that is different from that of the incident photon. The difference in energy between the incident photon and the scattered photon is absorbed by the molecule, which then occupies a vibrational state that is higher than its initial state. The energy difference between the incident and the emitted photon is equal to a molecular vibrational state. See specification at, *e.g.*, page 3, line 27 through page 4, line 25, and Figure 1.

Conventional Raman spectroscopy can be performed with a single laser. According to the presently claimed embodiments, however, Raman spectroscopy is *enhanced* by providing a second radiation source. The second radiation source is used to promote molecules in the analyte sample to a higher molecular vibrational state, such as the "Final (Stokes)" level shown in Figure 1 of the application. This promotion to a higher vibrational state increases the likelihood of a Raman excited molecule (*i.e.,* a molecule that has absorbed a photon from the first, Raman, laser) relaxing back down to the vibrational excited state. The result is an increase in the amplitude of a selected peak within the Raman spectrum. Accordingly, the instant claims specify that the "field generated by the second laser source matches a molecular vibrational energy state and thereby causes an enhanced Raman scattering effect of radiation of the first laser source". In other words, the second laser is selected to produce a field that enhances

normal Raman scattering as described above. Nowhere in the prior art can be found any suggestion whatsoever of such enhancement.

The first laser thus excites an electronic transition (discussed *supra*), as required to perform Raman scattering, whilst the second laser excites a vibrational transition (also discussed *supra*). By definition, the Raman-scattered photons have a frequency that is different from the frequency of the first laser (*e.g.*, specification at page 3, line 28 through page 4, line 5). Because, according to the instant embodiments, the molecular vibrational energy state, *i.e.*, the vibrational state of the Raman photon, (*e.g.*, specification at page 4, lines 6-25) is *matched* by the field generated by the second laser (*e.g.*, page 7, line 29 through page 8, line 17), it follows that the first and second radiation sources have differing frequencies.

Kreimer02, whether taken alone or in combination with any other knowledge in the prior art at the time of filing the present application, fails to teach or suggest that a second laser produces a field that matches a molecular vibrational energy state and causes an enhanced Raman scattering effect of the first laser. Kreimer02 further fails to teach or suggest that the two radiation sources described therein may have different frequencies. On the contrary, the general teaching of this document is that the two lasers should have the same frequency. Kreimer02 merely provides a way of performing SPR and SERS at the same time. According to Kreimer02 there is no synergy between the two techniques, nor is there any scintilla of a suggestion there or anywhere else in the prior art that the second laser may be arranged to enhance the SERS signal produced by the first laser. At most, Kreimer02 is limited to the suggestion (Kreimer02, paragraph 0006) that the two techniques (SERS, SPR) may be used to validate each other, from which the skilled person would understand that they are independent of one another. Where the PTO concedes that Kreimer fails to teach a second laser source, and where Chan merely teaches microfluid channels and so is at best cumulative with knowledge in the art, these documents fail to remedy the deficiencies of Kreimer02.

Applicants therefore submit that the PTO has not established a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 1339, 1341-43 (Fed. Cir. 1997), PTO has the burden of showing *prima facie* obviousness). The PTO must show that all of the claimed elements were known in the prior art, that a person skilled in the art could have combined the elements as

claimed by known methods with no change in their respective functions, and that the combination would have yielded nothing more than predictable results to such a skilled person. *KSR International Co. v. Teleflex Inc.*, 550 U.S. __,__, 127 S.Ct. 1727, 82 USPQ2d 1385, 1395 (2007), No. 04-1350 4, 14, (U.S. April 30, 2007). Additionally, the PTO must show that the person skilled in the art would have had a reasonable expectation of success in arriving at the claimed subject matter. M.P.E.P. § 2143.02 (citing *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986)).

In the instant case, including for reasons given above, it is submitted that the PTO fails to provide evidence or reasoning as to why the skilled person would reasonably have expected, much less reasonably expected *successfully,* to combine the recited elements. In brief, the role of the second laser to enhance a particular Raman peak is disclosed for the first time in the present application, as described above. By contrast, nowhere in Kreimer, Kreimer02, Chan and/or any other prior art knowledge can be found even a hint at the enhancement of the Raman scattering effect according to the instant claims. Applicants submit that the skilled person would not reasonably have expected to make the leap, from simply performing SERS and SPR independently of each other, to the present embodiments in which a second laser is specifically chosen to match a molecular vibrational energy state to obtain an enhanced Raman scattering effect.

Applicants submit further that "[a]ll words in a claim must be considered in judging the patentability of the claim against the prior art." *In re Wilson,* 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). See M.P.E.P. §2143.03. As such, when taken as a whole the subject matter of the instant claims is readily distinguishable over any teachings or suggestions of the prior art, where the interrelatedness of the recited elements in the claimed combination is clearly not even remotely contemplated by the prior art. Moreover, the United States Supreme Court recently opined on the obviousness standard: "A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art." *KSR International Co. v. Teleflex Inc.*, 550 U.S. __,__, 127 S.Ct. 1727, 82 USPQ2d 1385, 1395 (2007), No. 04-1350 4, 14, (U.S. April 30, 2007). Applicants therefore submit that the present claims are non-obvious even if the individual elements were independently known,

because their combination into the recited embodiments yielded the unexpected result of enhancing the Raman effect as discussed above.

With regard to the rejections of claims 40, 41 and 58-60 over Kreimer in view of Chan, and of claims 40-42 and 58-60 over Kreimer in view of Kreimer02 and further in view of Chan, it is submitted that for reasons given above, the rejections of the independent claims from which these claims depend have been overcome, such that the rejections of these dependent claims are no longer proper.

In view of the foregoing, it is submitted that the present claims fully comply with the requirements of 35 U.S.C. §103. Reconsideration and withdrawal of all rejections are therefore respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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